Drinking Distilled. Onset, course and treatment of alcohol use disorders in the general population
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Chapter 4

Predicting persistency of DSM-5 alcohol use disorder and examining drinking patterns of recently remitted individuals: a prospective general population study
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ABSTRACT

Aims
To establish the 3-year persistency rate of alcohol use disorder (AUD) and its predictors, and to examine drinking patterns of recently remitted individuals.

Design and setting
The Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2) surveyed a nationally representative sample of adults (aged 18-64) at baseline (response: 65.1%) and 3-year follow-up (response: 80.4%).

Participants
People with AUD at baseline, as defined by DSM-5 (n = 198).

Measurements
AUD, drinking patterns and mental disorders were assessed using the Composite International Diagnostic Interview 3.0. Other predictors were assessed with an additional questionnaire. Predictors of persistency were examined with univariable and multivariable logistic regression analyses.

Results
The AUD persistency rate was 29.5% (95% confidence intervals (CI) = 20.0; 39.0). In the multivariable model, the older (25-34 and 35-44) age groups had lower AUD persistency (odds ratio (OR) = 0.05, 95% CI = 0.00; 0.49 and OR = 0.14, 95% CI = 0.02; 0.79, respectively) than the youngest age group (18–24). A higher number of weekly drinks and a comorbid anxiety disorder predicted AUD persistency (OR = 1.03, 95% CI = 1.00; 1.07 and OR = 4.56, 95% CI = 1.04; 20.06, respectively). Furthermore, remission was associated with a reduction of six drinks per week between T₀ and T₁. It should be noted, however, that 35.8% (95% CI = 22.4; 49.2) of people in diagnostic remission still drank more than the recommended maximum (> 7/14 drinks weekly for women/men).

Conclusions
Only a minority of people in the Netherlands with alcohol use disorder as defined by DSM-5 still have the disorder three years later. Factors that help identify people at risk of alcohol use disorder persistence are: younger age, a higher number of weekly drinks and a comorbid anxiety disorder. A substantial number of people recently in diagnostic remission still drink above the maximum recommended level.

Marlous Tuithof, Margreet ten Have, Wim van den Brink, Wilma Vollebergh, Ron de Graaf
INTRODUCTION

Prospective studies on the course of alcohol use disorders (AUDs) in the general population have shown relatively low persistency rates (e.g. [1-4]), indicating that AUDs are persistent in some and transient in most people. However, persistent AUDs are often associated with high personal and societal costs [5-8] and may require expensive and intensive treatment [9;10]. Therefore, it is essential to identify people at risk of AUD persistency. Furthermore, diagnostic remission does not require a change in drinking patterns. Remitted individuals could thus still drink excessively and be at risk of health problems and relapse into another episode of AUD [11-14]. Unfortunately, it is largely unknown to which degree risky drinking still occurs in recently remitted people.

Epidemiological studies have observed several correlates of AUD persistency: male gender [15;16], younger age [16-18], being single [18], more AUD symptoms [19], severity of alcohol problems [3;15;20], more alcohol consumption [19], comorbid mood and anxiety disorders [3;18;21], comorbid drug dependence [3;16], personality disorders [16], smoking [18;19] and negative life events [22]. In contrast, correlates of a transient course included treatment utilization [23] and a longer AUD duration [1]. Interpretation of these findings is impeded, as most studies were cross-sectional, with a retrospective assessment of remission [1;16;18;22;23]. Other studies were longitudinal but used general population subsamples (e.g. men [20], young adults [3], anxious or depressed people [15;21]), thus preventing inferences about the general population. The only exceptions are longitudinal findings from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a prospective study including a nationally representative sample of US adults with a 3-year follow-up period [4;17;19]. Thus, more information derived from longitudinal population-based research seems desirable.

In previous studies, approximately one-quarter of people in remission from lifetime AUD currently had risky drinking patterns (for women defined > 7 drinks weekly or 4+ drinks on any day and for men > 14 drinks weekly or 5+ drinks on any day) [12;24]. They are at increased risk of alcohol-related diseases and relapse into another episode of AUD [12;13]. However, findings regarding lifetime remitters cannot be generalized to recent remitters. Specifically, as successful long-term remission is associated with lower drinking levels [12], conceivably a smaller proportion of risk drinkers is observed in lifetime, including long-term successful, remitters than in recent remitters. Thus, despite the overall decreased drinking levels associated with AUD remission [25], an important proportion may still drink excessively, and this subgroup is important for relapse prevention.

This study investigates predictors of AUD persistency and drinking patterns of recently remitted people. Using data from the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2), our aims are threefold: to (i) assess the 3-year AUD persistency rate in the general population; (ii) predict 3-year AUD persistency using a wide variety of predictors including sociodemographics, clinical AUD characteristics,
drinking characteristics, psychiatric comorbidity and vulnerability factors; and (iii) assess drinking patterns of people in recent diagnostic AUD remission. We hypothesize low persistency rates [1-4], but more persistency in those with more severe AUD (e.g. more AUD symptoms, higher alcohol consumption), psychiatric comorbidity and higher vulnerability (e.g. childhood abuse, negative life events). Finally, we expect that remitted cases show a 3-year decrease in drinking levels, but that more than one-quarter of them still has a risky drinking pattern. As validity of DSM-IV AUDs has been seriously criticized [26-32] regarding content and severity of criteria [26], presence of diagnostic orphans [27;28] and low validity of the alcohol abuse diagnosis [29-32], this paper uses DSM-5 AUD [33], which addressed most of these problems.

METHODS

Data were derived from two waves of NEMESIS-2 [34], a prospective epidemiologic survey in the general Dutch population. Baseline data (T₀) were collected in November 2007-July 2009. A multistage, stratified, random sampling procedure of households was applied with one respondent (aged 18-64), selected randomly from each household [34], resulting in a total sample of 6,646 adults (response: 65.1%). The 3-year follow-up wave (T₁) included 5,303 adults (response: 80.4%). Those who met criteria for DSM-5 AUD at T₀ (n = 198) were selected for the current study, of whom 155 (78.3% of T₀) were re-interviewed at T₁. No significant associations were found between baseline 12-month DSM-IV mental disorders and attrition [35].

The Composite International Diagnostic Interview (CIDI) version 3.0 was used at both waves to determine drinking patterns and DSM-IV mental disorder diagnoses. The CIDI is a fully structured, lay administered, interview developed by the World Health Organization (WHO), which is used worldwide. Clinical reappraisal interviews showed that it has generally good validity [36].

Persistency of alcohol use disorder

DSM-IV alcohol abuse and dependence symptoms were assessed with the CIDI, which also assessed craving: “Did you ever experience a time when you often had such a strong desire to drink that you couldn’t stop yourself from taking a drink or found it difficult to think of anything else?”. DSM-5 AUD symptoms include 3 of the 4 DSM-IV alcohol abuse criteria (without legal problems), all 7 DSM-IV alcohol dependence criteria and a new criterion covering craving [33]. DSM-5 AUD is diagnosed when ≥ 2 out of these 11 symptoms are present. Moreover, three severity levels are distinguished: mild (2-3 symptoms), moderate (4-5 symptoms) and severe (≥ 6 symptoms) [33]. All DSM-5 AUD symptoms were assessed using the CIDI 3.0. However, this instrument does not assess the DSM-5 clustering criterion (≥ 2 symptoms in the same 12-month period). Therefore, a symptom count was used to construct the diagnosis [37;38] and associated
severity levels. Persistency of AUD was defined as ≥ 2 DSM-5 AUD symptoms in the past 12 months at both T₀ and T₁.

**Predictors of persistency**
All predictors were recorded at T₀ except parental psychiatric history, which was assessed at T₁.

Sociodemographics included gender, age, low educational level (primary, basic vocational or lower secondary education), living without a partner, not having children at home, being unemployed, not having enough income to live on and living in an urban area.

AUD and drinking characteristics included the number of 12-month DSM-5 AUD symptoms, mean impairment in four areas of role functioning due to AUD (assessed with the Sheehan Disability Scale [39]), age of AUD onset, number of years that AUD was present (duration) and usual number of weekly drinks (see below).

Psychiatric comorbidity included 12-month mood disorder (major depression, dysthymia, bipolar disorder), anxiety disorder (panic disorder, agoraphobia, social phobia, specific phobia, generalized anxiety disorder), drug use disorder (drug abuse or dependence), and antisocial personality disorder.

Vulnerability factors were: smoking in the four weeks prior to the interview, lifetime parental history of depression/anxiety or of alcohol/drug addiction, mean number of 12-month negative life events (0-10) [40], having experienced psychological or physical abuse (more than once) or sexual abuse (once or more) before age 16, any 12-month service utilization and presence of a chronic somatic disease treated by a medical doctor in the previous 12 months.

**Change in alcohol consumption**
Mean number of weekly drinks at T₀ and T₁ were computed by multiplying answers to two questions: “In the past 12 months, how often did you usually have at least one drink – every day, nearly every day, 3-4 days a week, 1-2 days a week, 1-3 days a month, or less than once a month?” and “On the days you drank in the past 12 months, about how many drinks did you usually have per day?” Next, three variables regarding 3-year change in alcohol consumption were calculated: mean difference in number of weekly drinks (continuous), decrease in weekly alcohol consumption between T₀ and T₁ (yes/no) and increase in weekly alcohol consumption between T₀ and T₁ (yes/no).

A categorical variable representing three T₁ drinking categories was constructed: low-risk drinking (≤ 7/14 drinks weekly for women/men), moderate-risk drinking (8-14/15-21 drinks weekly for women/men) and high-risk drinking (> 14/21 drinks weekly for women/men). Additionally, a variable representing severe excessive alcohol consumption at T₁ was constructed including high-risk drinkers who also reported at least three 5+ drinking days a week [37].
Statistical analyses

First, the AUD persistency rate was established, as well as the prevalence rates and means of possible baseline predictors of 3-year AUD persistency. Secondly, these predictors were examined with univariable logistic regression analyses resulting in odds ratios (ORs) with 95% confidence intervals (CI). Thirdly, all predictors significant at $p < 0.10$ in univariable analyses were entered into a multivariable regression model to test them in relation to each other. McFadden’s pseudo $R^2$ was computed for the multivariable model. Finally, the association between AUD persistency and alcohol consumption was examined while adjusting for gender and age.

Some predictors had missing data (six variables with two missing values and one with 24 missing values) and there was attrition of 43 respondents (21.7% of $T_0$) between $T_0$ and $T_1$. As complete case analyses may introduce bias, missing values were imputed using multiple imputation by chained equations. All predictor and outcome variables and some additional variables associated with attrition were used for the imputation. Using 800 imputation cycles, we imputed 20 datasets [41].

Analyses were performed using Stata version 12.1 [42]. All logistic regression models were adjusted for the number of days between respondents’ $T_0$ and $T_1$ interview. The data were weighted to correct for baseline differences in response rates in subpopulations and in the probability of selection of respondents within households.

RESULTS

Sample description

Sample characteristics are portrayed in Table 4.1. On average, people with 12-month AUD at $T_0$ reported 3.3 AUD symptoms. Particularly, 69.3% had a mild, 17.3% a moderate and 13.4% a severe AUD. Functional disability due to AUD was fairly low, 1.2 on a scale from 0 to 10. Mean age of AUD onset was 21.3 and AUD duration was, on average, 10.4 years. Mean number of weekly drinks was 21.7.

Univariable predictors of persistency

Of the complete cases with baseline AUD ($n = 155$), 40 respondents still fulfilled the criteria of the disorder in the 12 months prior to $T_1$, corresponding with a weighted persistency rate of 30.9%. The imputed persistency rate was 29.5% (95% CI = 20.0; 39.0). Results of imputed data analyses showed that, on average, people with persistent AUD reported 4.2 AUD symptoms at $T_1$ and 57.2% of them had mild, 17.8% moderate and 24.9% severe AUD. Female gender, low educational level, living without a partner and not having children at home predicted persistency. Compared to the youngest (18-24), the older (25-34 and 35-44) age categories were at lower risk of AUD persistency. Also, persistency risk increased with more 12-month DSM-5 AUD symptoms, AUD disability and weekly drinks. In contrast, a longer AUD duration
Table 4.1. Baseline predictors of 3-year persistency of DSM-5 alcohol use disorder (AUD) in weighted column percentages or weighted means and weighted odds ratios (ORs) with 95% confidence intervals (95% CI) in people with baseline AUD (n = 198).

<table>
<thead>
<tr>
<th>Sociodemographics (%)</th>
<th>Total</th>
<th>No persistency</th>
<th>Persistency</th>
<th>AUD persistency univariable analyses</th>
<th>AUD persistency multivariable analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% / mean</td>
<td>% / mean</td>
<td>% / mean</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>Gender: male</strong></td>
<td>70.1</td>
<td>76.6</td>
<td>54.3</td>
<td>0.36* (0.15; 0.86)</td>
<td>0.47 (0.11; 1.96)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24 (ref)</td>
<td>28.0</td>
<td>16.7</td>
<td>54.9</td>
<td>1.00 -</td>
<td>1.00 -</td>
</tr>
<tr>
<td>25-34</td>
<td>28.2</td>
<td>36.8</td>
<td>7.7</td>
<td>0.06** (0.01; 0.35)</td>
<td>0.05* (0.00; 0.49)</td>
</tr>
<tr>
<td>35-44</td>
<td>21.6</td>
<td>25.7</td>
<td>11.8</td>
<td>0.14** (0.04; 0.57)</td>
<td>0.14* (0.02; 0.79)</td>
</tr>
<tr>
<td>45-64</td>
<td>22.2</td>
<td>20.8</td>
<td>25.6</td>
<td>0.37+ (0.12; 1.19)</td>
<td>0.36 (0.06; 2.16)</td>
</tr>
<tr>
<td>Low educational level</td>
<td>31.5</td>
<td>23.5</td>
<td>50.3</td>
<td>3.22* (1.06; 9.78)</td>
<td>1.70 (0.30; 9.54)</td>
</tr>
<tr>
<td>Living without a partner</td>
<td>62.6</td>
<td>55.9</td>
<td>78.6</td>
<td>2.89* (1.14; 7.30)</td>
<td>0.72 (0.16; 3.17)</td>
</tr>
<tr>
<td>No children at home</td>
<td>76.4</td>
<td>70.4</td>
<td>90.6</td>
<td>4.40* (1.17; 16.46)</td>
<td>1.93 (0.39; 9.44)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>21.2</td>
<td>18.1</td>
<td>28.3</td>
<td>1.64 (0.51; 5.29)</td>
<td>-</td>
</tr>
<tr>
<td>Not having enough income to live on</td>
<td>14.4</td>
<td>10.7</td>
<td>23.4</td>
<td>2.71 (0.76; 9.60)</td>
<td>- -</td>
</tr>
<tr>
<td>Urbanization: urban</td>
<td>71.0</td>
<td>71.0</td>
<td>71.0</td>
<td>1.04 (0.37; 2.91)</td>
<td>-</td>
</tr>
</tbody>
</table>

**Characteristics of AUD and drinking (mean)**

| DSM-5 12-month AUD symptom count (2-11) | 3.3 | 2.8 | 4.5 | 1.55*** (1.21; 1.99) | 1.37 (0.87; 2.15) |
| Disability due to AUD (0-10)            | 1.2 | 1.0 | 1.9 | 1.38* (1.06; 1.80)   | 0.82 (0.45; 1.48) |
| Onset of AUD                            | 21.3 | 21.3 | 21.3 | 1.00 (0.95; 1.05) | - - |
| Duration of AUD                         | 10.4 | 12.2 | 6.4  | 0.92** (0.86; 0.97) | 0.95 (0.90; 1.02) |
| Number of weekly drinks                 | 21.7 | 17.9 | 30.9 | 1.03** (1.01; 1.05) | 1.03* (1.00; 1.07) |

*Table 4.1 continues on the next page.*
Table 4.1. Baseline predictors of 3-year persistency of DSM-5 alcohol use disorder (AUD) in weighted column percentages or weighted means and weighted odds ratios (ORs) with 95% confidence intervals (95% CI) in people with baseline AUD (n = 198).

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>No persistency</th>
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<th>AUD persistency univariable analyses</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% / mean</td>
<td>% / mean</td>
<td>% / mean</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>Psychiatric comorbidity (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-month mood disorder</td>
<td>14.6</td>
<td>9.7</td>
<td>26.4</td>
<td>3.04* (0.93; 9.92)</td>
<td>1.61 (0.22; 12.03)</td>
</tr>
<tr>
<td>12-month anxiety disorder</td>
<td>27.4</td>
<td>20.1</td>
<td>45.0</td>
<td>3.19* (1.02; 9.97)</td>
<td>4.56* (1.04; 20.06)</td>
</tr>
<tr>
<td>12-month drug use disorder</td>
<td>11.9</td>
<td>11.4</td>
<td>13.0</td>
<td>1.14 (0.21; 6.12)</td>
<td>-</td>
</tr>
<tr>
<td>Antisocial personality disorder</td>
<td>12.0</td>
<td>7.7</td>
<td>22.1</td>
<td>3.97+ (0.89; 17.68)</td>
<td>0.63 (0.06; 6.08)</td>
</tr>
<tr>
<td><strong>Other vulnerability factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>60.4</td>
<td>57.4</td>
<td>67.2</td>
<td>1.51 (0.62; 3.68)</td>
<td>-</td>
</tr>
<tr>
<td>Parental history of depression/anxiety (%)</td>
<td>38.1</td>
<td>36.3</td>
<td>42.4</td>
<td>1.22 (0.48; 3.11)</td>
<td>-</td>
</tr>
<tr>
<td>Parental history of alcohol/drug addiction (%)</td>
<td>22.6</td>
<td>22.9</td>
<td>21.9</td>
<td>0.94 (0.32; 2.80)</td>
<td>-</td>
</tr>
<tr>
<td>Mean number of negative life events (0-10)</td>
<td>1.3</td>
<td>1.1</td>
<td>1.9</td>
<td>1.35* (1.05; 1.74)</td>
<td>0.91 (0.65; 1.27)</td>
</tr>
<tr>
<td>Childhood psychological abuse (%)</td>
<td>31.7</td>
<td>33.7</td>
<td>26.7</td>
<td>0.75 (0.28; 2.03)</td>
<td>-</td>
</tr>
<tr>
<td>Childhood physical abuse (%)</td>
<td>13.6</td>
<td>14.8</td>
<td>11.0</td>
<td>0.70 (0.16; 3.05)</td>
<td>-</td>
</tr>
<tr>
<td>Childhood sexual abuse (%)</td>
<td>9.4</td>
<td>9.3</td>
<td>9.4</td>
<td>0.96 (0.12; 7.60)</td>
<td>-</td>
</tr>
<tr>
<td>Any 12-month service utilization (%)</td>
<td>20.7</td>
<td>19.3</td>
<td>24.1</td>
<td>1.30 (0.39; 4.26)</td>
<td>-</td>
</tr>
<tr>
<td>Chronic somatic disease (%)</td>
<td>28.3</td>
<td>29.8</td>
<td>24.4</td>
<td>0.83 (0.26; 2.62)</td>
<td>-</td>
</tr>
</tbody>
</table>

Note. – Not calculated; + p < 0.10; * p < 0.05; ** p < 0.01; *** p < 0.001. All predictors that had p < 0.10 in the univariable analyses were included in the multivariable analyses.
decreased this risk. Comorbid anxiety disorder and a higher number of negative life events predicted persistency.

**Multivariable predictors of persistency**

All predictors significant at $p < 0.10$ in the univariable analyses were included in the multivariable analyses. Compared to the youngest age group, the older (25-34 and 35-44) age categories were still at decreased risk of AUD persistency. Furthermore, a higher number of weekly drinks increased the risk of AUD persistency. The presence of a comorbid anxiety disorder increased this risk almost fivefold. Notably, the number of 12-month DSM-5 AUD symptoms was no longer associated significantly with persistency. The pseudo $R^2$ of the multivariable model was 25.2%.

**Alcohol consumption and AUD persistency**

Of all remitted persons, 61% showed a decrease and 24% an increase in the number of weekly drinks (Table 4.2) resulting in a mean reduction of 6 drinks per week between $T_0$ and $T_1$. In comparison, 51% of the people with a persistent AUD showed a decrease and 43% an increase in the number of weekly drinks, with an overall increase of 10 drinks per week.

**Table 4.2.** Three-year change in alcohol use and follow-up ($T_1$) alcohol use by persistency of DSM-5 alcohol use disorder (AUD) in weighted column percentages or weighted means and weighted odds ratios (ORs) with 95% confidence intervals (95% CI) in people with baseline AUD ($n = 198$).

<table>
<thead>
<tr>
<th>Total</th>
<th>No persistency</th>
<th>Persistency</th>
<th>AUD persistency</th>
</tr>
</thead>
<tbody>
<tr>
<td>%/mean</td>
<td>%/mean</td>
<td>%/mean</td>
<td>OR (95% CI)</td>
</tr>
</tbody>
</table>

**3-year change in alcohol use**

- Mean difference in number of weekly drinks: -1.0 -5.5 9.6 1.04* (1.01; 1.06)
- Decrease in number of weekly drinks (%): 58.2 61.1 51.1 0.56 (0.20; 1.56)
- Increase in number of weekly drinks (%): 29.8 24.0 43.4 2.63 (0.90; 7.62)

**$T_1$ alcohol use**

- Mean number of weekly drinks: 20.6 12.4 40.5 1.07** (1.03; 1.12)
- Amount of drinking (%)
  - Low-risk drinking: 51.3 64.2 20.3 1.00 -
  - Moderate-risk drinking: 22.0 20.3 26.4 4.48* (1.22; 16.40)
  - High-risk drinking: 26.6 15.5 53.2 14.69*** (3.92; 54.99)
  - Excessive alcohol consumption (%): 15.7 7.7 34.9 10.66*** (2.98; 38.17)

*Note.* *p < 0.05; **p < 0.01; ***p < 0.001. Low-risk drinking: ≤7/14 drinks weekly for women/men; Moderate-risk drinking: 8-14/15-21 drinks weekly for women/men; High-risk drinking: >14/21 drinks weekly for women/men; Excessive alcohol consumption: high-risk drinking and at least three 5+ drinking days a week. ORs were adjusted for age and gender.
On average, remitted individuals drank moderately, as shown by both the mean number of weekly drinks (12) and the proportion of low-risk drinking (64.2%). Low-risk drinkers can be divided further into a small group with abstention (no alcohol consumed: 9.2%) and a much larger group with low-risk drinking (≤ 7/14 drinks weekly for women/men: 55.0%). Nonetheless, 35.8% (95% CI = 22.4; 49.2) of the remitted individuals still drank considerably. Specifically, 20% drank at moderate risk, 16% at high risk and 8% met our criteria of excessive alcohol consumption, as they also had at least three 5+ drinking days per week. However, the group with persistent AUD drank much more: on average 41 drinks per week and 26% drank at moderate-risk, 53% at high-risk and 35% met criteria for excessive alcohol consumption.

**DISCUSSION**

**Key findings**

The 3-year AUD persistency rate was 29.5%, confirming the relatively low persistency rates in previous epidemiological research (e.g. [1-4]) with the new DSM-5 definition. Factors that could help to identify people at risk of AUD persistency were: younger age, a higher number of weekly drinks and comorbid anxiety disorder. Furthermore, 36% remitted individuals still drank considerably (> 7/14 drinks weekly for women/men), which puts them at risk of physical and mental harm related to excessive alcohol consumption [11-14].

**Limitations**

As alcohol consumption and AUD diagnosis were based on self-report, recall bias might be an issue. For example, regarding alcohol consumption, people may have difficulty remembering the amounts and frequencies in an average week which may have resulted in a biased estimate, most probably an underestimation of alcohol consumption [43].

In prospective studies, the validity of findings can be affected adversely by sample attrition [44-46]. However, in a previous report on NEMESIS-2, no such bias was found for DSM-IV mental disorders [35]. Additionally, as multiple imputation was used to deal with missing data, we assume that sample attrition has had little effect on the presented findings.

The DSM-5 clustering criterion (≥ 2 symptoms in the same 12-month period) was not assessed and therefore we used a symptom count to generate the AUD diagnosis [37;38]. This may have resulted in an overestimation of prevalence rates and an underestimation of AUD persistency. However, the bias is possibly limited because the presence of multiple symptoms has been associated with poor outcomes, regardless of 12-month clustering [47]. More importantly, the CIDI 3.0 was designed and validated with regard to DSM-IV AUDs [36] and not DSM-5 AUD. Although the criteria used in DSM-IV and DSM-5 are largely the same, the reliability of the DSM-5 AUD diagnosis
Persistency of alcohol use disorder based on the CIDI 3.0 is unknown and could be lower than for DSM-IV, which may have resulted in a somewhat lower AUD persistency rate.

The number of subjects with DSM-5 AUD at baseline was limited, resulting in limited power in current analyses, thus precluding detection of smaller effects. Also, it was not possible to examine whether predictors of AUD persistency played a differential role in subgroups such as females, young adults or those with severe AUD.

Similar to previous studies [4;15], AUD persistency was regarded to be present if respondents reported 12-month AUD at both waves. Other longitudinal studies, including NESARC, used other definitions of persistency, such as the presence of at least one 12-month AUD symptom [20;21], including 12-month high-risk drinking [19] or the presence of AUD at any time between measurements [2;17]; or remission was divided in abstinent and non-abstinent remission [19]. Additionally, the follow-up period varied greatly among studies (range: 2-40 years [2-4,15,17,19-21,24]). These and other methodological differences hinder a direct comparison of findings.

Findings

Even though the 3-year persistency of DSM-5 AUD was quite low (30%), it was higher than persistency of DSM-IV alcohol abuse (15%) and dependence (25%) observed in a previous Dutch epidemiological study using a similar design and the same follow-up period [2]. These differences in persistency may be real differences, but may also reflect differences in CIDI 3.0 or DSM definitions. Nevertheless, confirming previous epidemiological research [48], it was observed in the present study that the vast majority of people with DSM-5 AUD had a mild form of AUD, which is likely to be associated with low levels of disability. This suggests, in combination with the low persistency rates, that an AUD diagnosis may not be clinically relevant for most people in the general population. It therefore seems imperative to use targeted interventions and to focus on those at risk of an unfavorable course.

Contrasting other studies [15;16], female gender predicted AUD persistency in the univariable analyses. Notably, a recent literature review observed that females in younger birth cohorts have a higher risk of AUDs than females in older birth cohorts [49]. Moreover, females have more severe AUD than males [50]. As we also observed that being in the youngest age group (18-24) predicted AUD persistency [16-18], this raises the question of whether or not risk of persistency may be strongest for females in the youngest age group. Post-hoc analyses confirmed this notion, as the persistency rate was much higher for young females (84%) than for older females (23%) or young (42%) or older males (17%). As young adults are obtaining an education or starting their career, alcohol problems at this age may seriously damage their prospect and thus attention for alcohol-related problems in young females seems desirable.

As hypothesized, more T0 AUD symptoms [19], more AUD-related disability [3;15;20] and more weekly drinks [19] increased the risk of AUD persistency. Notably, only the number of weekly drinks remained a significant predictor in the multivariable model.
This may be due to limited statistical power, especially because only a small proportion of the subjects had a severe baseline AUD in terms of number of symptoms or AUD-related disability. However, it also suggests that number of weekly drinks predicts a severe AUD course independent of AUD severity. Future studies should thus consider both AUD severity and alcohol consumption to increase comprehension of the dynamics of AUDs [37]. Remarkably, in the univariable analyses, a longer duration of AUD decreased the risk of persistency. This finding seems counterintuitive, but is in accordance with previous observations [1]. Conceivably, it is caused by the high persistency rate in the youngest age group, for whom a long AUD duration is not yet possible.

Comorbid anxiety disorder was a powerful predictor of AUD persistency [51]. Anxiety disorders may predict AUD persistency because they are associated with more severe AUD or higher alcohol consumption. However, the stronger association between anxiety disorders and AUD persistency in the multivariable model contradicts this explanation. Alternatively, anxious people use alcohol to alleviate anxiety; i.e. as a form of self-medication [52;53], and therefore alcohol problems more often persist. A similar relation was expected with regard to mood disorders and AUD persistency [3;18;54], but although we observed more persistency in those with a mood disorder, this association was not statistically significant. Nevertheless, these findings indicate that people with an AUD should be monitored for symptoms of other mental disorders [55;56], as interventions targeting these symptoms could also prevent a more severe course of AUD.

The number of negative life events was the only vulnerability factor that increased persistency risk [22]. Post-hoc analyses showed that of the specific life events, only serious problems with someone important or financial difficulties increased this risk. Contrasting other studies [1;18;19;23], none of the other vulnerability factors (smoking, parental psychiatric history, abuse before age 16, service utilization and chronic somatic disease) were associated significantly with AUD persistency.

Drinking patterns of people with a remitted AUD changed in accordance with our expectations: remission was associated with decreased drinking levels, although only 9.2% abstained, indicating that a reduction in risk-drinking is more important for remission than abstinence per se [57]. Notably, 20% of those in diagnostic remission reported moderate-risk drinking and 16% high-risk drinking. As remitted individuals with continued excessive drinking patterns have an increased risk of relapse [12;13], it seems desirable that prevention of relapse focuses on this group. Unfortunately, the limited number of remitted individuals hindered us to identify characteristics associated with risk drinking while being in remission. Nevertheless, this finding suggests that no longer fulfilling DSM-5 AUD diagnostic criteria is necessary but not sufficient to define remission. Lastly, a significant part of those with a persisting AUD did not drink excessively. Although striking, this is in accordance with previous cross-sectional findings based on the same dataset [37]. As post-hoc analyses showed that the DSM-5 severity levels were gradually associated with the number of weekly drinks, it seems desirable to
take both DSM-5 severity and actual alcohol consumption into account when examining severity of the disorder.

Implications
In a large prospective population-based study fewer than one-third of the people with baseline AUD still had the disorder at 3-year follow-up. Interventions, including prevention strategies [58], should therefore pay extra attention to those at highest risk of persistency, namely younger people, and especially young women, with AUD and people with a comorbid anxiety disorder [10;52]. Furthermore, the number of weekly drinks was a predictor of a persistent course regardless of the number of AUD symptoms or AUD-related disability and could thus also be used to identify people at risk of persistency. Finally, it should be noted that people in recent diagnostic remission from AUD may still drink considerably with continued health-related risks and an increased risk of relapse. To help improve targeted relapse prevention, future studies should examine predictors of excessive drinking after diagnostic remission.

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